PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Serial No. 09/694,241

In re patent Application of

Nicole BARIE et al.

Filed: October 23, 2000

For: DEXTRAN-COATED SURFACE

Confirmation No.: 9230

Group Art Unit: 1641

Examiner: Kartic Padmanabhan

APPEAL BRIEF TRANSMITTAL

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

Attached hereto is a copy of our Brief on Appeal in the above-identified application.

Also attached hereto is our Check No. 392447 in the amount of Five Hundred Dollars ($500.00) for the Brief fee. In the event this check should become detached, please debit our Deposit Account No. 160331 as needed in order to effect proper filing of this Brief.

Respectfully submitted,

STEPTOE & JOHNSON LLP

May 18, 2005
Date

Charles A. Wendel
Registration No. 24,453

Attorney Docket No. CSEM:065
STEPTOE & JOHNSON LLP
1330 Connecticut Ave., N.W.
Washington, D.C. 20036
(202) 429-6415

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BRIEF ON APPEAL

STEPTOE & JOHNSON LLP
1330 Connecticut Ave, N.W.
Washington, D. C. 20036
(202) 429-6415

TABLE OF CONTENTS

		Page
I.	REAL PARTIES IN INTEREST	1
II.	RELATED APPEALS AND INTERFERENCES	1
III.	STATUS OF CLAIMS	1
IV.	STATUS OF AMENDMENTS	2
V.	SUMMARY OF CLAIMED SUBJECT MATTER	2
VI.	GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL	3
VII.	ARGUMENT	3
	The Invention Generally and the General Relationship of the References Thereto	3
	Swan et al. '056	4
	Hubbell et al. '914	8
	Chai-Gao et al. '802	8
	Wessa et al. '631	10
	The Comments in the Advisory Action mailed March 3, 2005 Confirm the Error in the Examiner's Reasoning	10
VIII.	CONCLUSION	12

I. REAL PARTIES IN INTEREST

The real parties in interest are FORSCHUNGSZENTRUM KARLSRUHE GMBH (FZK), a German corporation, and CENTRE SUISSE d'ELECTRONIQUE ET DE MICROTECNIQUE S.A. (CSEM), a Swiss corporation, whose ownership interests are shown in an Assignment recorded on January 8, 2001 at Reel 011411, Frame 0167.

II. RELATED APPEALS AND INTERFERENCES

There are no prior or pending appeals, interferences or judicial proceedings known to appellants, the assignees or the undersigned that may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

The application was filed with ten claims. Claims 1, 3, 5, and 8 to 10 were amended in a reply filed July 7, 2004. Claims 1, 3, and 5 were further amended while claims 2 and 4 were canceled and claims 11 to 15 were added in an Amendment Under 37 CFR 1.116 filed November 17, 2004. Claims 1, 2, 4 and 5 were canceled and claims 3, 6, 8, 10 and 15 were amended in a Reply filed December 15, 2003. Claim 3 was further amended in a Supplemental Amendment filed January 9, 2004. Claims 11 to 15 were canceled in an Amendment Under 37 CFR 1.111 filed November 2, 2004 and claim 3 was again amended in an Amendment Under 37 CFR 1.116 filed February 17, 2005. The claims before the Board for consideration thus are claims 3 and 6 to 10.

IV. STATUS OF AMENDMENTS

The Amendment Under 37 CFR 1.116 filed February 17, 2005 has been entered and the claims read as they appear in the Appendix to this Brief.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The invention in the claims on appeal relate to a dextran-coated carrier having a surface with a connection between dextran disposed as a coating on the carrier formed by a photolinker. Claim 3 (the only independent claim) also specifies that the dextran coating is formed on and covalently attached to the carrier by co-immobilization resulting from a mixture of dextran and a 3-trifluoromethyl-3-m-isothiocyanophenyl diazirine (TRIMID)-modified aminodextran, the dextran being attached to the carrier through a component resulting from the irridiation of the 3-trifluoromethyl 3-m-isothiocyanophenyl diazirine (TRIMID)-modified aminodextran. The Board is directed to Fig. 1 which shows how dextran is linked to the carrier, in this instance a polyimide. See also the discussion in the specification at page 4, line 31 to page 6, line 11. The specification at page 5, lines 30 to 33 informs the reader that "the triplett carbenes formed during the irradiation can provide for cross-links with the protective layer as well as with the dextrans. In this way, the dextran becomes covalently attached to the surface." Fig. 1 shows such an arrangement and claim 3 specifies such an arrangement.

The dextran-coated surface is useful in the formation of a biosensor in which a receptive biomolecule is immobilized on the dextran; see the discussion in the specification at page 6, line 12 to page 8, line 19.

An advantage of the present invention is that dextran in the claimed environment can suppress non-specific binding. See the discussion in the last paragraph of the specification on page 8.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Two grounds of rejection are before the Board for review. The first rejection is that of claims 3 and 6 under 35 USC 103 as unpatentable over Swan et al. U.S. 5,563,056 or Hubbell et al. U.S. 5,529,914 in view of Chai-Gao et al. U.S. 5,858,802. The second ground of rejection for review is that of claims 3 and 6 to 10 (all claims on appeal) under 35 USC 103 as unpatentable over Swan et al. '056 or Hubbell et al. '914 in view of Wessa et al. WO 097/43631.

VII. ARGUMENT

The coating techniques taught in the primary references do not properly teach to a person of ordinary skill in the art what is required to form a dextran-coated carrier claimed herein and the secondary references do not provide disclosure sufficient to make the combination plausible. Indeed, the references are not properly combinable.

The Invention Generally and the General Relationship of the References Thereto

The claimed subject matter is directed to a dextran-coated surface formed in a manner represented by instant Fig. 1; see the discussion above in Section V. Fig. 1 shows a substrate, a polyimide there, having dextran attached thereto through the intermediary of a TRIMID--modified protein; in the figure, the protein is BSA making the intermediary T-BSA. The

references in combination do not teach or suggest the claimed invention. The references are improperly combined and no prima facie case of obviousness has been made.

Swan et al. '056

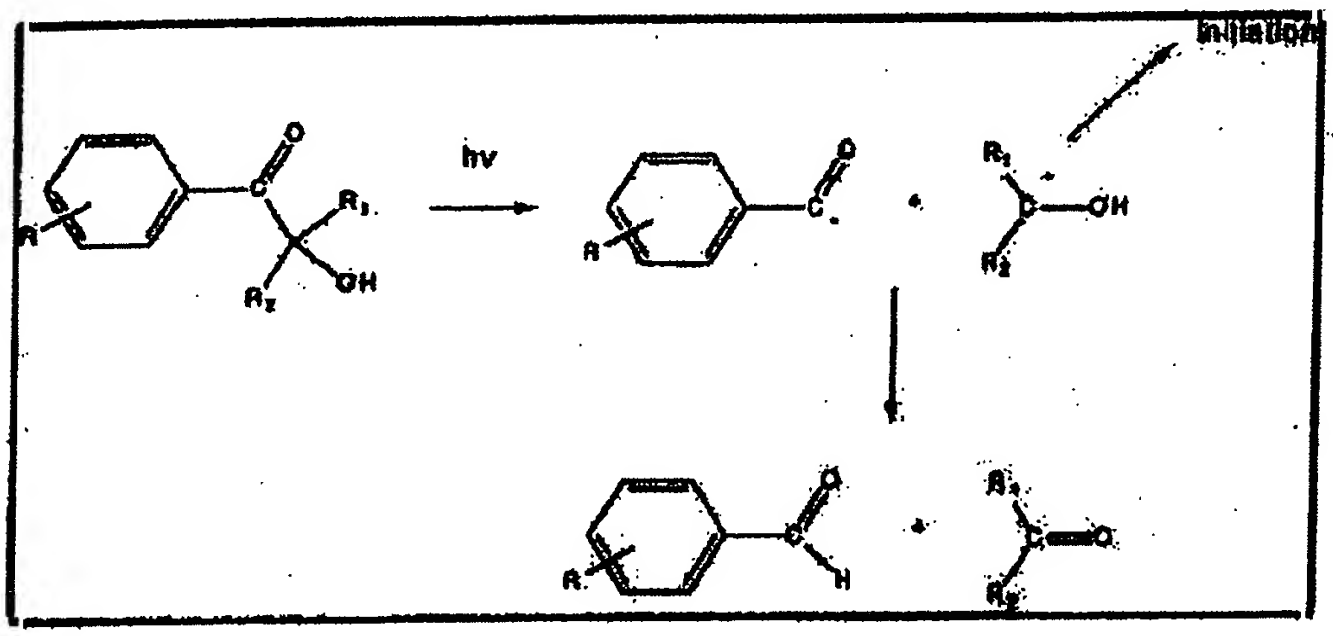
Swan et al. '056 describes various crosslinked matrices having covalently immobilized chemical species and unbound releasable chemical species (see the title) to provide release of one of those chemical species from the matrix; see the second-to-last sentence of the Abstract. The matrix is a three-dimensional one so it may achieve the intended purposes of the Swan et al. '056 invention. The matrix of the reference is a self-contained unit; see, for example, the last sentence of the Abstract and column 8, lines 56 to 65.

The reference discloses as an example of the first or second chemical species (which may also be regarded as the immobilized (bound) or unbound species) dextran sulfate (see the next-to-last subparagraph of patent claim 12) and lists various materials including organic polymers (see the last subparagraph of patent claim 12) as coupling compounds. There is no disclosure in the reference of the use of a protein, modified or not, as a coupling compound and there is no mention in the reference of dextran alone as a material to be connected. The last line of column 7 of the patent indicates that dextran sulfate is a carbohydrate useful for chromatography media. The patent further contains a discussion of using dextran sulfate as a chemical specie in combination with a coupling compound to bring those materials into "association permitting ionic attraction between them to pre-orient the chemical specie and the polymeric coupling compound with respect to each other before they are covalently bonded"; see

column 9, line 66 to column 10, line 4. Patent Example 12 (see columns 16 and 17) shows dextran sulfate (not dextran) co-immobilized onto polystyrene beads using a photoderivatized polyacrylamide made in Example 5 and a polyionic polymeric coupling compound made in Example 11. The connecting agent (the coupling compound) unquestionably is organic polymer based. Proteins, modified or not, are not disclosed as coupling compounds. The Examiner so acknowledges in the March 1, 2005 Advisory Action where line 6 of the Continuation of 11. section begins with the comment, "Applicant's arguments that Swan does not teach the use of a protein are accurate."

The Examiner has asserted throughout the course of prosecution that Swan et al. '056 discloses dextran as the polymer from which the "coupling compound" is derived. Dextran is not the "coupling compound" in the context of the present invention. The lack of Swan et al. '056's pertinence to the present invention is proven by the Examiner's remark. Swan et al. '056 is not related to the present invention.

Swan et al. '056 at column 11, lines 52 to 61, discusses the nature of the film surface that is to be covalently bonded by latent reactive groups of the coupling compound. It is stated at column 11, lines 58 to 61, that the surfaces "preferably have abstractable hydrogen atoms and participate readily in the formation of covalent bonds upon activation of the latent reactive groups." Forming covalent bonds involving hydrogen abstraction is applicable for photopolymerization initiated by photointermediates (ketyl) radicals generated, for instance, by benzophenone analogs which initiate propagating polymerization reactions in accordance with the following scheme.



In the present invention, use is made of reactive carbene intermediates generated from aryl diazirines. Carbenes form new covalent bonds by insertion into existing covalent bonds and do not initiate propagating polymerization reactions.

Carbenes undergo insertion reactions while the photoproducts of benzophenones bind to the materials by radical mediated processes, e.g., a generated ketyl radical may bind to a radical species formed on the surface material after hydrogen atom abstraction. With this step, new radicals are formed and polymerization continues until there is no more substrate providing abstractable hydrogen atoms. Covalent bonds are formed by radical to radical coupling. Such knowledge was known at the time of the Swan et al. '056 invention; see the copy of Optical Engineering (1995) 34-2339 to 2346, of record in the file.

The Examiner has stated that Swan at al. '056 discloses that dextran may be the coupling compound but appellants disagree. The reference lists various coupling compounds in claim 7 but neither dextran nor dextran sulfate appear. In contrast, both claim 2 and claim 5 of the patent list dextran sulfate as either as a first (trapped) or a second (diffusible) chemical species. One reading the patent without instant claim 3 as a point of reference would not find the patent to teach what it is asserted to teach. Appellants say that the infirmities of the reference acknowledged by the Examiner confirm the lack of pertinence of Swan et al. '056 to the instant invention.

HUBBELL ET AL. '914

Hubbell et al. '914 discloses ways to form biocompatible membranes around biological materials by the use of water-soluble molecules that are photopolymerized. For purposes of polymerization, the invention described in the reference uses materials called "macromers," which are described in detail at column 11 of the document. Listed as a macromer example are "ethylenically unsaturated derivatives" of dextran. Thus, the reference itself has no awareness, discussion, recognition, or understanding of using dextran itself as a material that is to be linked to a substrate. The only way in which dextran can be utilized for purposes of the Hubbell et al. '914 invention is as the central portion of an ethylenically unsaturated derivative of dextran. The reference also contains no mention of a protein, modified or otherwise, as a linker; the reference is believed not properly applicable here. Not only is the dextran used in Hubbell et al. '914 not dextran itself (rather the dextran is the central portion of an ethylenically unsaturated derivative of dextran), the Hubbell at al. '914 "dextran" is a "coupling component" rather than a material to be coupled. See the similar remarks above regarding the Examiner's discussion of dextran as a "coupling component" in the Swan at al. '056 invention.

The primary references as the Examiner acknowledges are very broad. They are so broad they do not direct the person of ordinary skill in the art to the invention in the claims on appeal.

CHAI-GAO ET AL. '802

Chai-Gao at al '802, while mentioning BSA and TRIMID, contains no example, let alone discussion, of using TRIMID-modified proteins and particularly TRIMID-modified BSA

as a co-immobilizer for dextran to a substrate. Chai-Gao et at. '802 has no mention of dextran and there is no proper reason to combine the references. The deficiencies of the primary references have been discussed previously. The secondary reference cannot and does not provide the focus needed to permit combination of that reference with the teachings of the primary references.

Moreover, it was well known from previous published experimental work that carbenes bind distinctly to all individual amino acids that may be present at the surface of a protein. That work is reported in the Journal of Photochemistry and Photobiology, B: Biology, 7, (1990) 277 to 287 entitled "Philicity of Amino Acid Side-Chains for Photogenerated Carbenes"; see the copy of this article in the file. A reading thereof shows that a carbene philicity scale was derived from the experiments reported therein and that carbene insertion (which leads to covalent bond formation) correlates with the polarity of the amino acid side chain and with the number of chemical bonds present in the side chain of the amino acid in question. Hydrophobic amino side chains are more carbene philic than hydrophilic amino acids and large amino acid side chains are also more carbene philic than small ones. The backbones of the dextran and aminodextran polymers consist of glucose monomers, meaning that the polymers are highly hydrophilic in nature. The molecular surface exposes many small hydrophilic hydroxyl functions. Tightly bound water molecules adhere to dextran and its derivatives. Thus, a person of skill in the art would not expect the dextran surface to be carbene philic.

Contrary to the expectations discussed above, appellants discovered and have claimed that dextran is immobilized and that modified aminodextran itself could be used as a photo-linker polymer. Thus, the assertion in the Advisory Action that the reference has been relied upon

merely "to cure this deficiency" (that Hubbell et al. '914 does not teach using a modified protein as a photolinker) is not properly based on what the references themselves teach or suggest.

WESSA ET AL. WO '631

Wessa et al. WO '631 describes a prior art technique involving TRIMID and T-BSA but the reference in no proper fashion teaches or suggests the subject matter of the claims.

Wessa et al. WO '631, which as the instant case has Dr. Hans Sigrist as a joint inventor, describes a prior art technique of covalently-linked (therefore not diffusible) carbene mediated immobilization of a biomolecule to a polyimide. (The Examiner states in the Advisory Action that Wessa et al. WO '631 was cited merely to show a protein. More is required to make the rejection a proper one. The art has to provide some reason for its combination.) The discussion taken with either Swan et al. '056 or Hubbell et al. '914 does not direct the person of ordinary skill in the art to the invention claimed here. The references have been cobbled together; they do not properly teach or suggest the invention claimed. The lighted path provided by hindsight and by hindsight only is the illumination used improperly in support of the rejections. Even in hindsight, the references do not suggest what is claimed here.

The Comments in the Advisory Action mailed March 3, 2005
Confirm the Error in the Examiner's Reasoning

Swan et al. '056 clearly shows dextran as part of a coupling material that has to contain "an average of at least two latent reactive groups per molecule"; see column 3, lines 40 to 41. Dextran per se has no latent reactive groups as defined in that reference. Moreover, it is believed clear from a reading of claim 3 on appeal that dextran is the compound to be immobilized and

that the coupling compound is 3-trifluoromethyl 3-misothiocyanophenyl diazirine (TRIMID) modified amino dextran.

The comment that "Hubbell et al. states that virtually any photoinitiator can be used with the method of their reference" is believed to be overly broad; see for example, claims 9 and 42 of the patent. Appellants note that Hubbell et al. '914 claims 1 and 35 state that photopolymerization is carried out in aqueous media, which means that irridiation of the photoinitiator also takes place in such media. Carbenes (the type of material subjected to photoinitiation in the present invention), when photogenerated in aqueous media, will undergo certain reactions with molecules and will not form covalent bonds with adjacent target molecules. Thus, the references do not and cannot properly lead to the present invention.

The Examiner also states that "the claims generically refer to dextran and do not exclude derivatives of dextran." Appellants disagree strong. The Amendment Under 37 CFR 1.116 filed February 17, 2005 expressly directed a change in claim 3 so that the claim reads in pertinent part "a connection between dextran ...." Thus, "the dextran" in the latter part of the claim is dextran mentioned above. The claim specifies dextran.

The rationales given in the Advisory Action establish clearly that the references when considered apart from the instant claims do not teach the invention on appeal. There is no proper reason to combine these references; no prima facie case of obviousness exists.

VIII. CONCLUSION

Claims 3 and 6 to 10 patentably define over the cited art for the reasons given above and the Board is asked to so hold.

Respectfully submitted,

STEPTOE & JOHNSON LLP

May 18, 2005
Date

Charles A. Wendel
Registration No. 24,453

Atty. Docket: CSEM:065

STEPTOE & JOHNSON LLP
1330 Connecticut Ave., N.W.
Washington, D.C. 20036
(202) 429-6415

APPENDIX

3. A dextran-coated carrier having a surface with a connection between dextran disposed as coating on the carrier formed by a photolinker, said dextran coating being formed on and covalently attached to said carrier by co-immobilization resulting from a mixture of the dextran and a 3-trifluoromethyl-3- (m-isothiocyanophenyl)-diazirine (TRIMID)-modified aminodextran, wherein the dextran is attached to the carrier through a component resulting from the irradiation of the 3-trifluoromethyl-3-(m-isothiocyanophenyl)- diazirine (TRIMID)-modified aminodextran.

6. A dextran-coated surface according to claim 3, wherein said carrier surface is coated with a polymer film.

7. A dextran-coated surface according to claim 6, wherein said polymer film consists of one of polyimide and poly-(p-xylylene).

8. A dextran-coated surface according to claim 3, wherein said carrier surface is a surface of a mass-sensitive sensor.

9. A dextran-coated surface according to claim 8, wherein said mass-sensitive sensor is surface acoustic waves conductive component.

10. A dextran-coated surface according to claim 3, wherein said carrier surface is a surface of an optical or electro-mechanical sensor.